42 Clinical characteristics of infants diagnosed through cystic fibrosis newborn screening (CF NBS)

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CF NBS in Poland started in 2006, the Warsaw CF Centre being responsible for 25% of the population (over 100,000 births a year). The screening protocol is based on IRT/DNA analysis, covering the 15 most common mutations as well as over 300 of the less common using sequencing technology.

Among the 43 infants disgnosed were 10 with meconium ileus – MI (only 2 did not have increased IRT values).

The average age of diagnosis was 46.6 days. Both mutations were known in 38 out of 43 infants. The most common were F508del homozygotes (44, 2%) and F508del heterozygotes (32.6%). In 5 patients only 1 mutation was found. Among MI infants 60% were F508del homozygotes. The average sweat test values were 68.9%. In 2 children sweat test values were lower than 40 mmol/l. There were 8 children who at the time of diagnosis were symptom free, 5 presented respiratory symptoms, 5 both: respiratory and gastrointestinal (GI), and 25 only GI syndroms (MI, steatorrhea, hiperbilirubinemia, worse somatic development). 30% of the patients were pancreatic sufficient. There were no radiological changes at x-ray on diagnosis. In 4 children *Pseudomonas aeruginosa* colonisation was confirmed in the first year of life.

Conclusions:

1. In most of the CF infants GI symptoms were observed at the time of diagnosis
2. Most of hte MI infants had increased IRT values and were detected through the normal screening protocol
3. In screened newborns positive sweat test should be established at 30 mmol/l
4. A larger spectrum of mutations enables diagnosis of CF even in infants with normal sweat tests.

43 Risk factors for poor outcomes in Cystic Fibrosis – 10 years of challenging experience in Eastern Europe

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Early diagnosis and treatment can improve survival in Cystic Fibrosis (CF).

Aim: to determine if certain risk factors (RF) may impact clinical outcomes.

Methods: Retrospective study of clinical files of CF patients (age range 0–24 years) followed up between 1999–2009 in a Children's Hospital. RF: late follow up after diagnosis (LFD), poor socioeconomic status (PSS), malnutrition at diagnosis (MD), del F508 homozygous(HDF), frequent pulmonary exacerbations(PE), early Paer colonization(EPC), associated conditions(AC) were correlated with clinical scores quantified at the time of file analysis. Funding for CF care since 2004 was taken into account in evaluation. Study population was divided in group A (25/38-diagnosis under the age of 1 year) and group B (5/38-after the age of 1 year), excluding meconium ileus (MI) patients.

Results: 10 patients died (70% before 2004, mean age at death 1.1 year).21% presented with MI and underwent surgery. Age when started follow up differed between groups (0.38 months vs.4.57 years)which impacted on recurrence of PE (53% vs 83%) ($p < 0.001$). 81% patients were genotyped; 57% of the 28 currently followed up were HDF. 35% (10/28)patients still had malnutrition at evaluation; this correlated in 35% (8/28) with PSS and negatively impacted on Schwachmann scores. Early CFLD (4/38), ABPA (2/38) and reintervention for complicated MI (6/8) influenced the outcomes. 85% patients had EPC. PE were more frequent in patients who associated PSS, MD, AC. Lung function was poorer over the study period in the late followed up patients with more RF.

Conclusion: Beyond early age at diagnosis and high standards of care-goals that have to be achieved, there are RF that may be influenced in order to improve the outlook of CF patients.

44 Comprehensive cost comparison of newborn screening strategies with novel inclusion of costs related to genetic counseling and collection of second specimens

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Great strides have been made in expansion of the CF newborn screening programs in the USA, to include all states by the year 2010. Three different protocols are currently in use throughout the states: IRT/IRT, IRT/DNA, and IRT/IRT/DNA. This study presents a comprehensive cost analysis and, for the first time, includes costs related to genetic counseling (GC), and collection of the 2nd dried blood specimen (2nd DBS) required in both the IRT/IRT and IRT/IRT/DNA screening algorithms. Other costs being included relate to differences in the numbers of sweat test referrals observed with each protocol and complete laboratory costs (equipment, reagents, courier services, space, information systems, overhead, and maintenance). With information obtained from a sample of states using each protocol, we created a model for cost comparison that included all of these elements. Preliminary analysis of cost data collected at the University of Kentucky related to the 2nd DBS for the IRT/IRT protocol demonstrated a cost increase of at least $0.16 per newborn. Analysis of GC cost data from Wisconsin, utilizing IRT/DNA, revealed an increase of $0.04 per newborn. Thus, our results demonstrate that GC is not a substantial cost barrier to implementation of IRT/DNA and is less than the 2nd DBS expenses. In conclusion, our findings suggest that the expenses for obtaining the 2nd DBS should be taken into account in regions using IRT/IRT and may be a higher system-wide cost than that for DNA analyses. Calculations related to IRT/IRT/DNA are still underway, as are further analyses to compare the cost-benefits of each protocol.

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45 Incidence of the CFTR exon 9 and its flanking sequence duplication on the mutation diagnosis in CF patients

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Since the CFTR gene cloning, more than 1500 genetic alterations have been so far described; most of them are disease-causing mutations. We present here two cases which have 1524+6insC+12G>A mutations in intron 9. In sequence database, several different regions were determined for the homology with the CFTR exon 9 and its intronic boundaries. The comparison of homologous sequences are 95–96% similar to each other, inducing the interference of our target sequence with other homologous sequences in human genome. Sequence alignment analysis reveals that five registered mutations in CF mutation database, http://www.genet.sickkids.on.ca/cftr, may be due to this similarity and prevent the correct screening of mutations. For this reason, we conclude from this statement that there are some pseudomutations resulting from the identity of CFTR exon 9 and its flanking regions with similar-related sequences in the human genome. Using specific PCR primers or high annealing temperature, we can amplify specifically the CFTR exon 9 region, and not the pseudogene sequences. We suggest that patients carring mutation in this region should be re-examined with our specific technique.

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